

### **REMARKS**

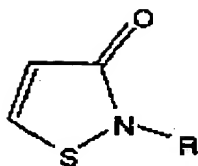
The final Official Action mailed March 25, 2003 has been received and carefully reviewed. Claims 1-27 are herein canceled and new claims 28-39 have been added which are drawn to Working Examples 1 and 4. In light of the amendments presented above, as well as for the reasons set forth below, reconsideration and withdrawal of the currently pending rejections is requested.

With regard to the Examiner's objection to claim 27 as being a substantial duplicate of claim 22, the above amendment canceling both claims is believed to obviate this rejection.

Further, with regard to the Examiner's rejection of claims 20, 22 and 27, under 35 U.S.C. § 112 (first paragraph), on the basis that the specification does not support the features of claims 20 and 22 in the recitation of the phrase "...Formula III produced contains less than 1.0% of 5-chloro-2-alkyl-4-isothiazoline-3-one," the Applicants have canceled claims 20, 22 and 27, and further replaced those with new claims 28-39 which set forth the process described in Working Examples 1 and 4 where the content of 5-chloro-2-alkyl-4-isothiazoline-3-one to less than 0.1% as shown in Table 2. Therefore, it is asserted that the Examiner's rejection of claims 20, 22 and 27, under § 112 (first paragraph), has been rendered moot.

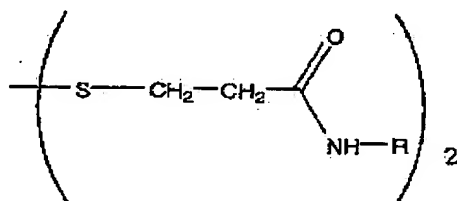
With regard to the Examiner's rejections of claims 1-27, under 35 U.S.C. 103(a), as being unpatentable over GB 2,308,364 to Kim et al. or U.S. Patent No. 3,849,430 to Lewis et al., each taken alone or in combination with each other, the Applicants continue to respectfully traverse each of this rejection for the reasons set forth in the Amendment of December 30, 2002. In addition to those reasons, the Applicants further state the following.

Independent claims 28, 34 and 37 set forth the following method steps for producing 2-alkyl-4-isothiazoline-3-one represented by the general Formula (III),

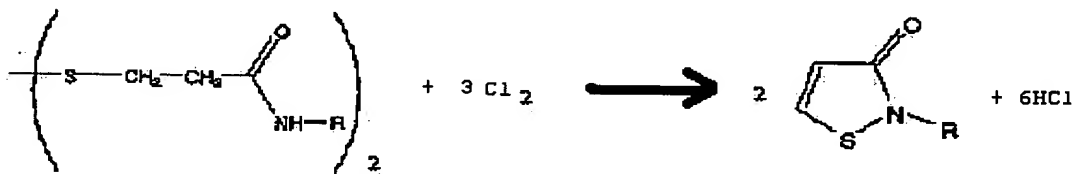


wherein the amount of mutagenic 5-chloro-2-alkyl-4-isothiazoline-3-one contained in the 2-alkyl-4-isothiazoline-3-one produced is less than 0.1%:

reacting the compound represented by Formula (II),



with chlorine as a chlorinating agent in dichloromethane as a solvent, in which hydrogen chloride is insoluble or exhibits low solubility, at a temperature of 39-41°C, according the reaction formula represented by:



wherein R in the compounds of formulae (II) and (III) represents an alkyl group or aralkyl group of C1 to C8, (Emphasis added)

In contrast, with regard to the Kim et al reference the Examiner states in repeating the rejection that Kim et al, in Scheme 5, pages 12-13, teach a process of making a biocidal 2-methyl-4-isothiazoline-3-one through the use of Cl<sub>2</sub> (or sulfonylchloride) as the chlorinating agent in combination with a mixed solvent system (some of which include those exemplified in the instant claims) for reaction with:

n-methyl-3-mercaptopropionamide (A-1), or  
N,N dimethyl 3,3'-dithiodipropionamide (A-2),

to yield a mixture of 2-methyl-4-isothiazoline-3-one (Formula I of Kim et al) and the mutagenic **5-chloro-2-methyl-4-isothiazolin-3-one (Formula II of Kim et al)**. The Applicants note that Kim et al sets forth **no** specific example of using Cl<sub>2</sub> with the dichloromethane solvent at a process temperature of 39-41°C as claimed to achieve 2-methyl-4-isothiazoline-3-one with essentially no (or <0.1%) 5-chloro-2-methyl-4-isothiazolin-3-one (II) as presently claimed. To the contrary, Kim et al contains specific guidance (see page 8, lines 1-3; page 9, lines 19-25; page 10, lines 2-10; page 11, lines 13-24) to carry out the process, regardless of solvent system or starting materials, at 5-20 °C to reduce the formation of the undesirable skin irritant 4, 5-dicholoro-2-methyl-4-isothazolin-3-one (III) (see Examples 1-22 of Table 1). Specifically, Kim et al state (page 11, lines 13-24) that reaction temperatures above 20 °C results in undesirable amounts of 4,5-dicholoro-2-methyl-4-isothazolin-3-one (III) (see Comparative Example 2 of Table 1). Therefore, one of ordinary skill in the prior art is provided by Kim et al with a clear motivation to carry out the disclosed process at 5-20 °C to produce a biocidal composition which contains **both** 2-methyl-4-isothiazoline-3-one (I) **and** the mutagenic 5-chloro-2-methyl-4-isothiazolin-3-one (II) to reduce the formation of the undesirable skin irritant 4,5-dicholoro-2-methyl-4-isothazolin-3-one (III).

In light of the failure of the Kim et al reference to teach the specifically claimed use of chlorine and the dichloromethane solvent in a reaction process carried out at 39-41°C to produce 2-alkyl (or aralkyl)-4-isothiazoline-3-one to the exclusion (less than 0.1%) of 5-chloro-2-alkyl-4-isothiazolin-3-one, one of ordinary skill in the prior art must look for some suggestion or motivation in Kim et al. to modify the teachings to arrive at the claimed process of forming the 2-methyl-4-isothiazoline-3-one over the mutagenic 5-chloro-2-methyl-4-isothiazolin-3-one. As mentioned above, that motivation to make such modification is non-existent in Kim et al and is in fact

contrary to the very specifically desired feature of Kim et al to carry out the process to form 2-methyl-4-isothiazoline-3-one **along with the mutagenic** 5-chloro-2-methyl-4-isothiazolin-3-one while reducing the presence of the skin irritant 4,5-dicholor-2-methyl-4-isothazolin-3-one (III).

As noted to the Examiner previously, in evaluating the teachings of the prior art the Examiner must consider all factors relating to the obviousness, including negative teachings or teachings away. See MPEP Chapter 2143.01 (particularly at pages 2100-124 & 125). In that regard, the teachings of Kim et al provide no guidance (teach away) so as to carry out the process of making a composition containing 2-methyl-4-isothiazoline-3-one without (less than 0.1%) with the mutagenic 5-chloro-2-methyl-4-isothiazolin-3-one, e.g., the Comparative Example 1 of Kim et al still teaches utilizing chlorine gas and ethyl acetate at 15 °C to form the mutagenic 5-chloro-2-methyl-4-isothiazolin-3-one **in preference to** 2-methyl-4-isothiazoline-3-one.

Since Kim et al alone does not teach or suggest to one of ordinary skill in the prior art to carry out the claimed process with any likelihood of success for the reasons advanced above, a rejection, under 35 U.S.C. 103(a), based upon Kim et al of the instantly claimed invention would be improper.

The Examiner attempts to remedy the deficiencies of Kim et al by additionally citing the Lewis et al reference, either taken alone or in combination with Kim et al, to render the claimed invention obvious.

With regard to the Lewis et al. reference, as mentioned in the earlier December 30, 2002 Amendment, the Examiner's position is that the patentees teach forming the 3-isothiazolones presently claimed by oxidation cyclization of either a disulfideamide of Formula III (which is the same as the claimed Formulae II) or a mercapto amide of Formula IV (which is the same as the claimed Formulae I) with a halogenating agent selected from the group of chlorine, bromine, sulfuryl chloride, sulfuryl bromide, N-chlorosuccinimide, N-bromosuccinimide, with chlorine and sulfuryl chloride being

preferred. The Examiner further asserts that the process of Lewis et al. is carried out in an inert, non-aqueous solvent such as benzene, toluene, xylene, ethyl acetate, ethylene dichloride, 1-nitropropane.

However, as highlighted above, independent claims 28, 34, and 37 set forth the features of reacting the starting material of Formula II with Cl<sub>2</sub> in a dichloromethane solvent at a process temperature of 39-41°C as claimed to achieve 2-methyl-4-isothiazoline-3-one with essentially no (or <0.1%) 5-chloro-2-methyl-4-isothiazolin-3-one, none of which are not explicitly taught or suggested by Lewis et al. That is, the Applicants respectfully assert that the teachings of Lewis et al alone, or in combination with Kim et al, do not render obvious the claimed method of forming the 3-isothiazolones of the claimed Formula III by reacting Formulae II (of claims 28, 34 or 37) with chlorine (Cl<sub>2</sub>) as a halogenating agent and in a dichloromethane solvent at process temperature of 39-41°C.

In that regard, the Applicants note that Lewis et al state that the temperature of cyclization is "not critical" and can be in the range of 0-100°C (column 3, lines 3-6), and the Applicants further note that the patentees present no examples of reacting the starting material of Formula II with chlorine in a dichloromethane solvent at the 39-41°C process temperature and present no guidance that the selection of the starting materials, reaction system and process temperature can be controlled to yield the presently claimed results, i.e., <0.1%) 5-chloro-2-methyl-4-isothiazolin-3-one. Perhaps that closest example of Lewis et al (Example 8) with regard to reaction temperature reacts a dithio-N,N-bis(n-decyl) dipropionamide with chlorine and a toluene solvent at 40-45°C to yield a 2-n-decyl-3-isothiazolone. However, since the starting materials are different from that presently claimed, little guidance is provided by Example 8 of Lewis et al with regard to the selection of the claimed starting materials, solvents and processing temperatures to form a compound of Formula III having essentially no (less than 0.1%) 5-chloro-2-methyl-4-isothiazolin-3-one (II). The remaining examples of Lewis et al utilize sulfuryl chloride (Examples 1-5, 7, 9-

12) or bromine (Example 6) or chlorine (Examples 13, 14) in ethylene dichloride or ethyl acetate at temperatures of 20-30°C and provide no guidance as to the selection of starting materials or temperatures to achieve the claimed formation of Formula III having essentially no (less than 0.1%) 5-chloro-2-methyl-4-isothiazolin-3-one (II). It is of note that the instant Working Examples 1 and 4, when carried out at temperatures of 22-30°C yield 5-chloro-2-methyl-4-isothiazolin-3-one in amounts above 0.1%, e.g., 0.6%. (While the Applicants are of the opinion that such information is not necessary to find that the teachings of Kim et al or Lewis et al do not render obvious the presently claimed invention, if the Examiner is of the opinion that such data, submitted in declaration form, would be necessary to a finding patentability of the instant claims, it is requested that the Examiner set forth that requirement in the next Office Action.)

Since, for the above reasons, Lewis et al alone does not teach or suggest to one of ordinary skill in the prior art to carry out the instantly claimed process with any likelihood of success for the reasons advanced above, a rejection, under 35 U.S.C. 103(a), based upon Lewis et al of the instantly claimed invention would be improper.

Finally, as pointed out above, neither Kim et al. nor Lewis et al. alone explicitly or implicitly teach all the claimed features, and when combined would clearly teach (see Kim et al) one of ordinary skill in the prior art to carry out the cyclization process from 2-methyl-4-isothiazoline-3-one along with the 5-chloro-2-methyl-4-isothiazolin-3-one for the advantageous biocidal properties (noted by both Kim et al and Lewis et al and emphasized by the Examiner). Therefore, upon evaluating all the evidence presented by the teachings of Kim et al and Lewis et, a *prima facie* case of obviousness with regard to the presently claimed invention has not been set forth by the Examiner since neither Kim et al or Lewis et al suggest modifying the teachings therein to react a compound of Formula II with chlorine (Cl<sub>2</sub>) in a dichloromethane solvent at 39-41°C to yield the compound of Formula III contains less than 0.1% of the mutagenic 5-chloro-2-alkyl-4-isthiazoline-3-one.

Consequently, a rejection, under 35 U.S.C. 103(a), based upon Kim et al in combination with Lewis et al should not be maintained with regard to claims 28-39.

In view of the foregoing, Applicants respectfully submit that the present application should now be in condition for allowance. The Examiner's reconsideration and withdrawal of the present rejections is respectfully requested. An early Notice of Allowance is courteously solicited. However, should the Examiner believe that there are further issues remaining to be resolved to place the application in condition for allowance, she is invited to contact the undersigned.

Respectfully submitted,

  
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